

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

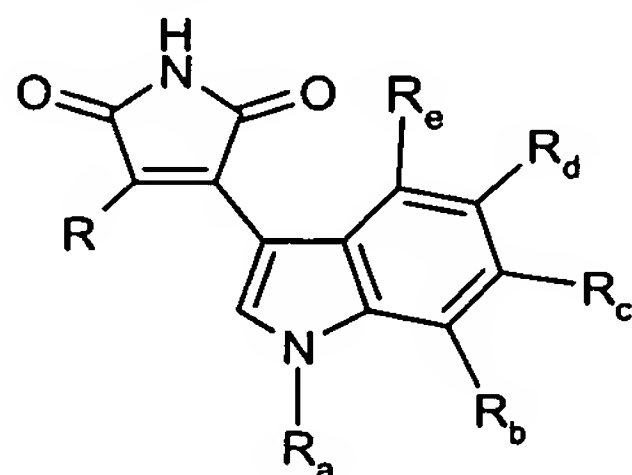
Claim 1. (Canceled)

Claim 2. (Currently amended): A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for the PKC over one or more protein kinases which do not belong to the CDK-family, and a selectivity for the PKC α , PKC β and optionally PKC θ , over one or more of the other PKC isoforms of at least 10 fold, as measured ~~according to claim 1~~ by the ratio of the IC₅₀ of the compound for a PKC which is not α and β , and optionally not θ , to the IC₅₀ of the compound for the PKC α , PKC β or PKC θ , respectively.

Claim 3. (Original): A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for PKC α , PKC β and optionally PKC θ , over one or more of the other PKC isoforms of at least 10 fold, and for which the ratio of the IC₅₀ value as determined by Allogeneic Mixed Lymphocyte Reaction (MLR) assay to the IC₅₀ value as determined by Bone Marrow proliferative (BM) assay is higher than 5.

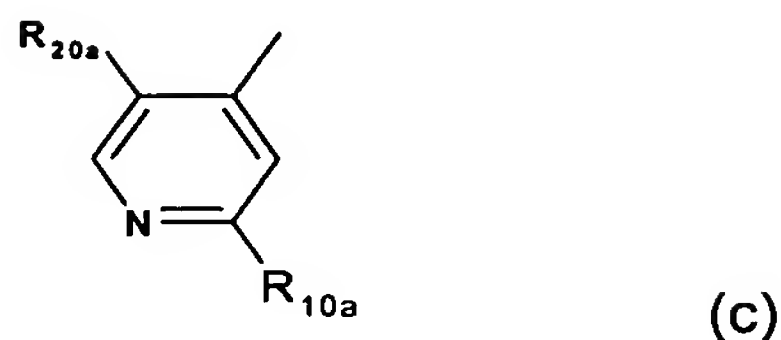
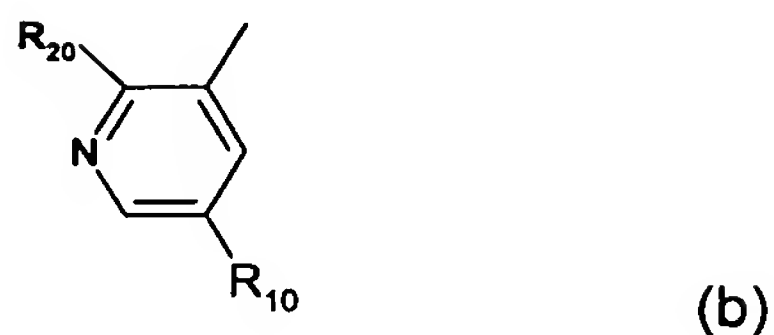
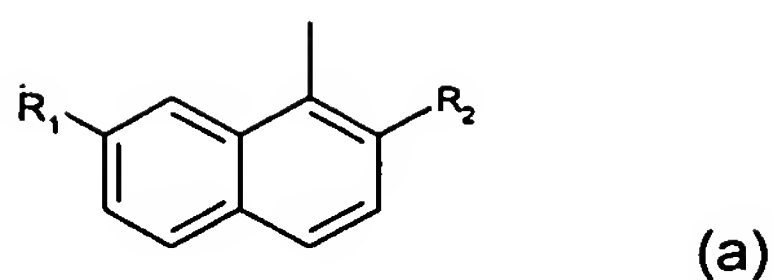
Claim 4. (Currently amended): A compound which is an inhibitor of the PKC, in free form or in a pharmaceutically acceptable salt form, wherein said compound possesses a selectivity for the PKC α , PKC β and PKC θ , over one or more of the other PKC isoforms of at least 10 fold, as measured according to claim ~~4~~2.

Claim 5. (Original): A compound of formula I



wherein

R_a is H; C₁₋₄alkyl; or C₁₋₄alkyl substituted by OH, NH₂, NHC₁₋₄alkyl or N(di-C₁₋₄alkyl)₂;
one of R_b, R_c, R_d and R_e is halogen; C₁₋₄alkoxy; C₁₋₄alkyl; CF₃ or CN and the other three substituents are each H; or R_b, R_c, R_d and R_e are all H; and
R is a radical of formula (a), (b) or (c)



wherein

R_1 is $-(CH_2)_n-NR_3R_4$,

wherein

each of R_3 and R_4 , independently, is H or C_{1-4} alkyl; or R_3 and R_4 form together with the nitrogen atom to which they are bound a heterocyclic residue;

n is 0, 1 or 2; and

R_2 is H; halogen; C_{1-4} alkyl; CF_3 ; OH; SH; NH_2 ; C_{1-4} alkoxy; C_{1-4} alkylthio; NHC_{1-4} alkyl; $N(di-C_{1-4}alkyl)_2$, CN, alkyne or NO_2 ;

wherein

each of R_{10} and R_{10a} , independently, is a heterocyclic residue; or a radical of formula α



wherein X is a direct bond, O, S or NR_{11} wherein R_{11} is H or C_{1-4} alkyl,

R_f is C_{1-4} alkylene or C_{1-4} alkylene wherein one CH_2 is replaced by CR_xR_y wherein one of R_x and R_y is H and the other is CH_3 , each of R_x and R_y is CH_3 or R_x and R_y form together $-CH_2-CH_2-$,

Y is bound to the terminal carbon atom and is selected from OH, $-NR_{30}R_{40}$ wherein each of R_{30} and R_{40} , independently, is H, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, aryl- C_{1-4} alkyl, heteroaryl- C_{1-4} alkyl, C_{2-6} alkenyl or C_{1-4} alkyl optionally substituted on the terminal carbon atom by OH, halogen, C_{1-4} alkoxy or $-NR_{50}R_{60}$ wherein each of R_{50} and R_{60} , independently, is H, C_{1-4} alkyl, C_{3-6} cycloalkyl, C_{3-6} cycloalkyl- C_{1-4} alkyl, aryl- C_{1-4} alkyl, or R_{30} and R_{40} form together with the nitrogen atom to which they are bound a heterocyclic residue; and

each of R_{20} and R_{20a} , independently, is H; halogen; C_{1-4} alkyl; C_{1-4} alkoxy; CF_3 ; nitrile; nitro or amino;

or a salt thereof.

Claim 6. (Original): A compound according to claim 5 wherein R_a is H or methyl; each of R_2 , R_{20} and R_{20a} , independently, is H, Cl, NO_2 , F, CF_3 or methyl, n is 0 or 1; one of R_b , R_c , R_d and R_e is methyl or ethyl and the other three substituents are H; or R_b , R_c , R_d and R_e are all H; and each of R_3 and R_4 , independently, is H, methyl, ethyl or *i*-propyl; or R_3 and R_4 form together with the nitrogen atom to which they are bound a heterocyclic residue optionally substituted; and each of R_1 , R_{10} and R_{10a} , independently, is a heterocyclic residue.

Claim 7. (Currently amended): A compound according to claim 5 or 6 which is selected from

3-[5-Chloro-2-(4-methyl-piperazin-1-yl)-pyridin-4-yl]-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-Chloro-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(6-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-methylaminomethyl-naphthalen-1-yl)-4-(5-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(6-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-dimethylaminomethyl-naphthalen-1-yl)-4-(5-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-{2-Chloro-7-[(ethyl-methyl-amino)-methyl]-naphthalen-1-yl}-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-diethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-ethylaminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-[2-Chloro-7-(isopropylamino-methyl)-naphthalen-1-yl]-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-[2-Chloro-7-(4-methyl-piperazin-1-ylmethyl) naphthalen-1-yl]-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(2-Chloro-7-pyrrolidin-1-ylmethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(1,7-dimethyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl-2-methyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;

3-(7-Aminomethyl -naphthalen-1-yl)-4-(1-H-indol-3-yl)-pyrrole-2,5-dione;
 3-(7-Aminomethyl-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
 3-(7-Amino-naphthalen-1-yl)-4-(1-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
 3-(7-Amino-naphthalen-1-yl)-4-(1H -indol-3-yl)-pyrrole-2,5-dione;
 3-(7-Dimethylaminomethyl-2-fluoro-naphthalen-1-yl)-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
 3-(7-dimethylaminomethyl-2-fluoro-naphthalen-1-yl)-4-(1H-indol-3-yl)-pyrrole-2,5-dione;
 3-(1-Methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(7-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(1-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-trifluoromethyl-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(7-methyl-1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[5-(4-methyl-piperazin-1-yl)-2-nitro-pyridin-3-yl]-pyrrole-2,5-dione;
 3-[2-chloro-5-(4-methyl-piperazin-1-yl)-pyridin-3-yl]-4-(7-methyl-1H-indol-3-yl)-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[5-methyl-2-(4-methyl-piperazin-1-yl)-pyridin-4-yl]-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[2-(4-methyl-piperazin-1-yl)-5-nitro-pyridin-4-yl]-pyrrole-2,5-dione;
 3-(1H-indol-3-yl)-4-[2-(4-methyl-piperazin-1-yl)-5-trifluoromethyl-pyridin-4-yl]-pyrrole-2,5-dione;
 in free form or in a pharmaceutically acceptable salt form.

Claim 8. (Currently amended): A compound according to ~~any one of claims 5 to 7~~, in free form or in a pharmaceutically acceptable salt form, for use as a pharmaceutical.

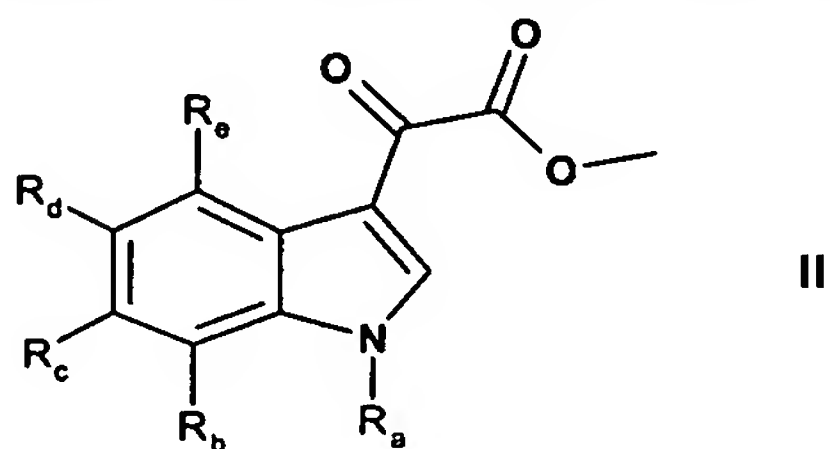
Claim 9. (Currently amended): A compound according to ~~any one of claims 2 to 7~~, for treating or preventing diseases or disorders mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer.

Claim 10. (Currently amended): A pharmaceutical composition comprising a compound according to ~~any one of claims 2 to 7~~, in free form or in pharmaceutically acceptable salt form, in association with a pharmaceutically acceptable diluent or carrier therefor.

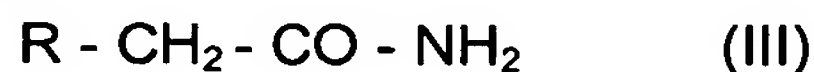
Claim 11. (Canceled)

Claim 12. (Currently amended): A pharmaceutical combination comprising a compound according to ~~any one of claims 2 to 7~~, in free form or in a pharmaceutically acceptable salt form, and a further agent selected from immunosuppressant, immunomodulatory, anti-inflammatory, chemotherapeutic, antiproliferative and anti-diabetic agents.

Claim 13. (Currently amended): A process for the production of a compound according to claim ~~5 or 6~~, which process comprises reacting a compound of formula II



wherein R_a to R_e are as defined in claim 5 ,
with a compound of formula III



wherein R is as defined in claim 5,
and, where required, converting the resulting compound of formula I obtained in free form to a salt form or vice versa, as appropriate.

Claim 14. (Currently amended): A method for treating or preventing disorders or diseases mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer, in a subject in need of such a treatment, which method comprises administering to said subject an effective amount of an inhibitor of PKC which possesses a selectivity for $PKC\alpha$, $PKC\beta$ and optionally $PKC\theta$, over one or more of the other PKC isoforms of at least 10 fold, as measured according to claim ~~4~~2, or a pharmaceutically acceptable salt thereof.

Claim ~~15~~17. (Currently amended): A method for treating or preventing disorders or diseases mediated by T lymphocytes and/or PKC, in particular allograft rejection, graft versus host disease, autoimmune diseases, infectious diseases, inflammatory diseases, cardiovascular diseases or cancer, in a subject in need of such a treatment, which method comprises administering to said subject an effective amount of a compound according to ~~any one of claims 2 to 7~~, or a pharmaceutically acceptable salt thereof.